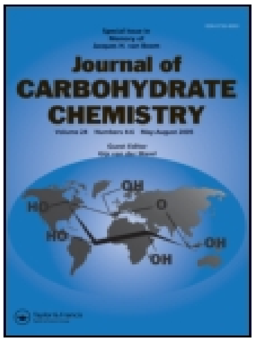


Taylor & Francis
Taylor & Francis Group

Journal of Carbohydrate Chemistry

ISSN: 0732-8303 (Print) 1532-2327 (Online) Journal homepage: http://www.tandfonline.com/loi/lcar20

Synthesis of a Blocked Tetrasaccharide Related to the Repeating Unit of the Antigen from Shigella dysenteriae Type 9 in the Form of Its Methyl (R)-Pyruvate Ester and 2-(Trimethylsilyl)Ethyl Glycoside

Samarpita Roy & Nirmolendu Roy

JOURNAL OF CARBOHYDRATE CHEMISTRY
Vol. 22, Nos. 7 & 8, pp. 521–535, 2003

Synthesis of a Blocked Tetrasaccharide Related to the Repeating Unit of the Antigen from *Shigella dysenteriae* Type 9 in the Form of Its Methyl (*R*)-Pyruvate Ester and 2-(Trimethylsilyl)Ethyl Glycoside†

Samarpita Roy and Nirmolendu Roy*

Department of Biological Chemistry, Indian Association for the Cultivation of Science, Jadavpur, Kolkata, India

ABSTRACT

Starting from D-mannose, D-galactose and D-glucosamine hydrochloride, two disaccharide blocks were synthesized. Schmidt's inverse addition technique of trichloroacetimidate was utilized for the construction of a disaccharide with a β-mannosidic linkage in good yield. The other disaccharide had a methyl 4,6-(*R*)-pyruvate ester. The two disaccharides in the appropriate form were then allowed to react in the presence of *N*-iodosuccinimide (NIS) and trifluoromethanesulfonic acid (TfOH) to give the desired tetrasaccharide derivative, 2-(trimethylsilyl)ethyl 2-acetamido-3,4,6-tri-*O*-benzoyl-2-deoxy-β-D-glucopyranosyl-(1 → 3)-2-*O*-benzoyl-4,6-*O*-[(*R*)-1-methoxycarbonylethylidene]-β-D-galactopyranosyl-(l → 4)-2,3,6-tri-*O*-benzyl-β-D-mannopyranosyl-(1 → 4)-2,6-di-*O*-benzyl-3-*O*-(4-methoxybenzyl)-β-D-galactopyranoside.

Key Words: Synthesis; Tetrasaccharide derivative; *Shigella dysenteriae* type 9.

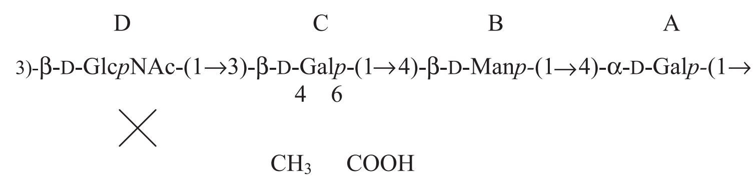
†This paper is dedicated to Professor Gérard Descotes on the occasion of his 70th birthday.

*Correspondence: Nirmolendu Roy, Department of Biological Chemistry, Indian Association for the Cultivation of Science, Jadavpur, Kolkata 700 032, India; E-mail: bcnr@mahendra.iacs.res.in.

DOI: 10.1081/CAR-120026456
0732-8303 (Print); 1532-2327 (Online)

INTRODUCTION

Shigella dysenteria type 9, a gram-negative pathogen, is one of the infective agents responsible for many intestinal diseases including dysentery. As carbohydrate-based antibacterial vaccines found increasing interest in recent years,[1,2] it is considered relevent to explore this approach for the preparation of vaccines against *Shigella dysenteria* type 9. A considerable amount of work has already been carried out in different laboratories,[3–8] including ours,[9,10] on the synthesis of carbohydrate haptens related to *Shigella*. We report herein the synthesis of a blocked tetrasaccharide derivative related to the repeating unit **I** of the antigen from *Shigella dysenteriae* type 9 in the form of its methyl (*R*)-pyruvate ester and 2-(trimethylsilyl)ethyl glycoside.[11,12]

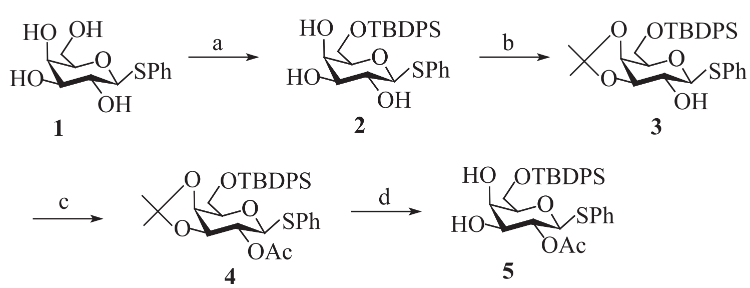


I

RESULTS AND DISCUSSION

Our strategy is to synthesize the blocks DC and BA as their stable derivatives, convert them to a suitable disaccharide donor and a disaccharide acceptor and finally allow them to react in the presence of an appropriate promoter.

Phenyl 1-thio-β-D-galactopyranoside[13] (**1**) was treated with *tert*-butyldiphenylsilyl chloride[14] (TBDPSCl) in pyridine to afford phenyl 6-*O*-*tert*-butyldiphenylsilyl-1-thio-β-D-galactopyranoside (**2**) which upon treatment with 2,2-dimethoxypropane[15] in *N*,*N*-dimethylformamide gave the 3,4-*O*-isopropylidene derivative **3**. The reason for introducing the TBDPS group before the 3,4-isopropylidene moiety was to avoid the formation of 4,6-isopropylidene derivative. Acetylation of **3** followed by removal of the isopropylidene group from the product **4** afford phenyl 2-*O*-acetyl-6-*O*-*tert*-butyldi-

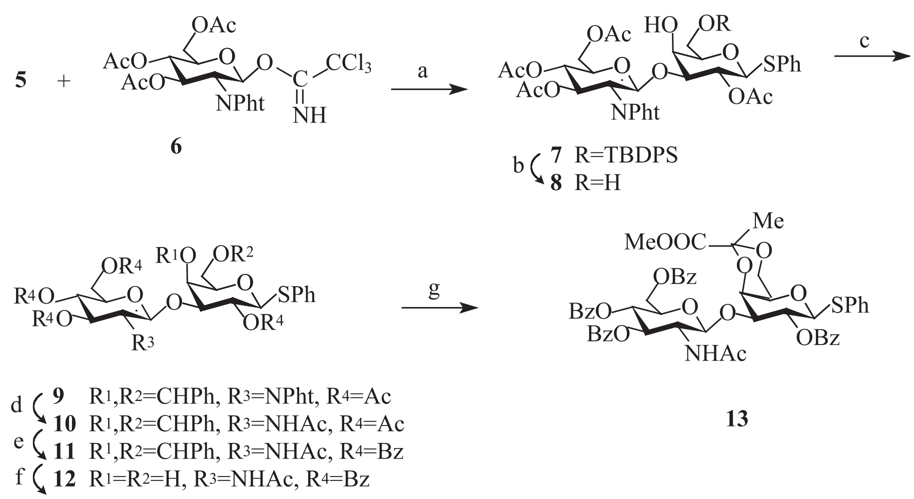


Scheme 1. a) TBDPSCl, Pyr, 2 h; b) DMP, CSA, DMF, 12 h; c) Ac_2O, Pyr, 3 h; d) 80% AcOH, 80°C, 1 h.

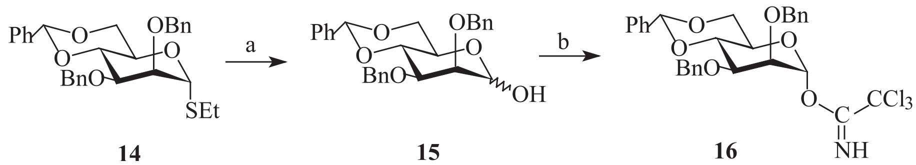
Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

phenylsilyl-1-thio-β-D-galactopyranoside (**5**) (Scheme 1). The structure of **5** was confirmed from its ^{1}H and ^{13}C NMR spectra.

The acceptor **5** with two hydroxyl groups of different reactivity was then allowed to react with the known 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl trichloroacetimidate[16] (**6**) in the presence of triethylsilyltrifluoromethanesulfonate (TESOTf) in dichloromethane at −20°C to afford phenyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1 → 3)-2-*O*-acetyl-6-*O*-(*tert*-butyldiphenylsilyl)-1-thio-β-D-galactopyranoside (**7**) in 71% yield. Compound **7** has characteristic signals for a phthalimido group, 4 acetyl groups, TBDPS and C-2 together with anomeric protons and carbons in the NMR spectra. The formation of the 1 → 3 linked disaccharide was confirmed by acetylation of **7**, giving a product which showed a downfield shift of the signal for H-4^{C} from δ 4.14 to 5.39 in the corresponding ^{1}H NMR spectrum. Removal of TBDPS group[17] from **7** using tetrabutylammonium fluoride (TBAF) in tetrahydrofuran gave **8**, which upon treatment with α,α-dimethoxytoluene[18] and 10-camphorsulphonic acid (CSA) in acetonitrile afforded phenyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1 → 3)-2-*O*-acetyl-4,6-*O*-benzylidene-1-thio-β-D-galactopyranoside (**9**) in 88% yield. Treatment of **9** with ethylenediamine in 1-butanol,[19] followed by reaction of the product thus formed with acetic anhydride and pyridine, gave phenyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl-(1 → 3)-2-*O*-acetyl-4,6-*O*-benzylidene-1-thio-β-D-galactopyranoside (**10**) in 89% yield. Deacetylation of **10** followed by benzoylation of the product afforded the corresponding tetrabenzoate **11**. Replacement of the acetyl group with benzoyl was effected because of the greater stability of the benzoate during the pyruvate acetal formation[20] involved in the next step. Removal of the benzylidene from **11** gave **12** which was treated with pyruvic acid methyl ester[20,21] and borontrifluoride etherate in acetonitrile



Scheme 2. a) TESOTf, CH_2Cl_2, −30°C, 2 h; b) TBAF, THF, 0°C, 6 h; c) α,α-DMT, CH_3CN, camphorsulfonic acid, 2 h; d) i. n-BuOH, $NH_2CH_2CH_2NH_2$, 90°C, 20 h; ii. Ac_2O, pyridine; e) i. NaOMe, MeOH, 1 h; ii. BzCl, pyridine, 0°C, 4 h; f) 80% AcOH, 70°C, 1 h; g) $CH_3COCOOMe$, $BF_3.OEt_2$, CH_3CN, 3 h.



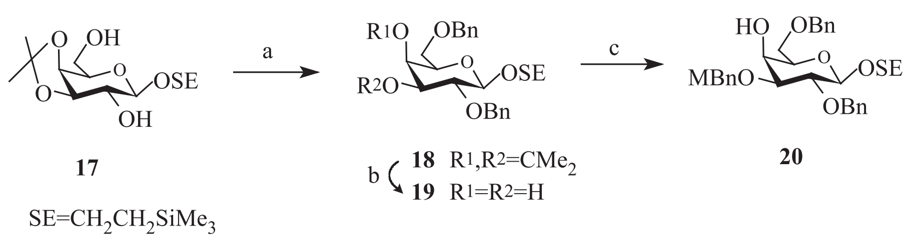
Scheme 3. a) $Hg(OCOCF_3)_2$, H_2O, CH_2Cl_2, 0°C, 12 h; b) CCl_3CN, K_2CO_3, CH_2Cl_2, 5 h.

to afford phenyl 2-acetamido-3,4,6-tri-*O*-benzoyl-2-deoxy-β-D-glucopyranosyl-(1 → 3)-2-*O*-benzoyl-4,6-*O*-[(*R*)-1-methoxycarbonylethylidene]-1-thio-β-D-galactopyranoside (**13**) in 65% yield (Scheme 2) as the 6:1 (*R*) and (*S*) mixture from which a reasonable quantity of pure (*R*) was separated by repeated column chromatography and utilized for next step. The structure of **13** was confirmed from its signals for pyruvate acetal, NHAc and anomeric protons and carbons in its NMR spectra. The (*R*) configuration of **13** was confirmed[21] from the ^{13}C NMR signal of CH_3 group at δ 25.8. The corresponding (*S*) configuration of the pyruvate gave CH_3 signal at δ 18.1.

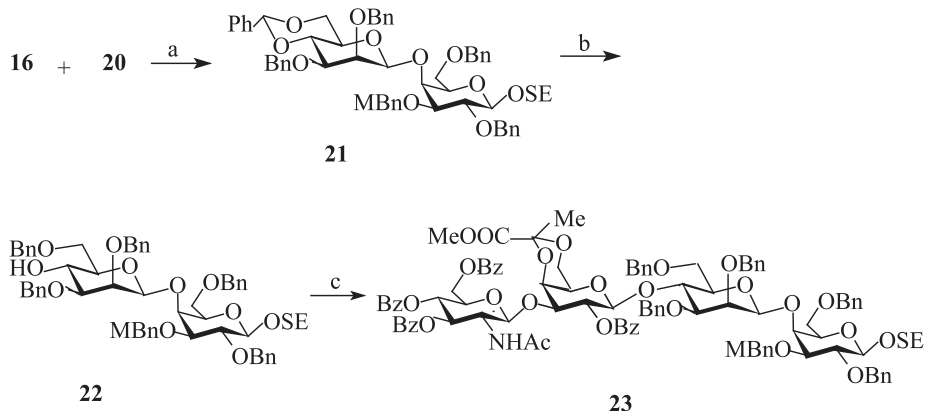
In a separate experiment, the thioethyl group in the anomeric position of the known ethyl 4,6-*O*-benzylidene-2,3-di-*O*-benzyl-1-thio-α-D-mannopyranoside[22] (**14**) was removed with mercury(II) trifluoroacetate[23] in moist dichloromethane and the product **15** was transformed into the donor 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranosyl trichloroacetimidate[24] (**16**) with trichloroacetonitrile in the presence of potassium carbonate (Scheme 3). About 10% of β-trichloroacetimidate was also formed as revealed from the ^1H NMR spectrum of the product.

In another experiment, benzylation of 2-(trimethylsilyl)ethyl 3,4-*O*-isopropylidene-β-D-galactopyranoside (**17**) prepared from the known 2-(trimethylsilyl)ethyl β-D-galactopyranoside[25] gave the dibenzyl derivative which on treatment with 80% acetic acid afforded **19** with two free hydroxyl groups. Regioselective 4-methoxybenzylation of **19** via the stannylene derivative[26] afforded 2-(trimethylsilyl)ethyl 2,6-di-*O*-benzyl-3-*O*-(4-methoxybenzyl)-β-D-galactopyranoside (**20**) (Scheme 4). The NMR spectra of compound **20** show characteristic signals for OCH_3 and OCH_2CH_2Si as well as the anomeric proton and carbon.

The mannopyranosyl trichloroacetimidate donor **16** was allowed to react with the acceptor **20** in dichloromethane at −45°C in the presence of 0.15 equivalent of TESOTf under inverse condition.[24] Indeed the trichloroacetimidate donor was being added to



Scheme 4. a) BnBr, NaH, DMF, 6 h; b) 80% aq AcOH, 80°C, 1 h; c) i. Bu_2SnO, C_6H_6, reflux, 8 h; ii. 4-Methoxybenzyl chloride, TBAB, 63°C, 6 h.



Scheme 5. a) TESOTf, CH_2Cl_2, −30°C, 2 h; b) $NaBH_3CN$, $HCl.OEt_2$, 0°C, 10 min: c) **13**, NIS, TfOH, −10°C, 25 min.

the mixture of acceptor and TESOTf, to afford the disaccharide 2-(trimethylsilyl)ethyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-mannopyranosyl-(1 → 4)-2,6-di-*O*-benzyl-3-*O*-(4-methoxybenzyl)-β-D-galactopyranoside (**21**) in 84% yield with 1:5 ratio of α and β anomers. The β-anomer could be easily separated from the mixture by column chromatography. The structure of **21** was confirmed from the NMR signals characteristic for benzylidene, OMBn, OSE and the anomeric regions. Moreover, the coupling constants ($J_{1,2} < 0.5$ Hz, $J_{2,3} = 3.0$ Hz and $J_{3,4} = 10.1$ Hz) of the β-mannose residue in **21** support the mannose configuration.[27] Regioselective opening of the benzylidene ring[26] of **21** afforded the disaccharide acceptor **22** (Scheme 5).

The disaccharide donor **13** was then allowed to react with the disaccharide acceptor **22** in the presense of *N*-iodosuccinimide (NIS) and trifluoromethanesulfonic acid[28] (TfOH) in dichloromethane to afford the tetrasaccharide derivative 2-(trimethylsilyl)ethyl 2-acetamido-3,4,6-tri-*O*-benzoyl-2-deoxy-β-D-glucopyranosyl-(1 → 3)-2-*O*-benzoyl-4,6-*O*-[(*R*)-1-methoxycarbonylethylidene]-β-D-galactopyranosyl-(1 → 4)-2,3,6-tri-*O*-benzyl-β-D-mannopyranosyl-(1 → 4)-2,6-di-*O*-benzyl-3-*O*-(4-methoxybenzyl)-β-D-galactopyranoside (**23**) in 66% yield (Scheme 5). Compound **23** was characterized, based on the presence of NMR signals for NHAc, methyl pyruvate, OMBn and anomeric regions.

In summary, we have developed a method for the synthesis of the blocked tetrasaccharide derivative related to the repeating unit of the O-antigen from *Shigella dysenteriae* type 9 in the form of its methyl 4,6-(*R*)-pyruvate ester and 2-(trimethylsilyl)ethyl glycoside. It is possible to utilize this tetrasaccharide derivative for the preparation of glycoconjugates.

EXPERIMENTAL

General. All reactions were monitored by TLC on Silica Gel G (E. Merck). Column chromatography were performed on 100–200 mesh Silica Gel (SRL, India) using 15–20 times (by weight) of the crude product. The organic extracts were dried over anhydrous Na_2SO_4. All solvents were distilled and/or dried before use and all evaporations were conducted at or below 40°C under reduced pressure unless stated otherwise. Optical rotations were measured at 25°C with a Perkin-Elmer 241 MC polarimeter. The ^{1}H and ^{13}C NMR spectra were recorded with a Bruker DPX 300 spectrometer using $CDCl_3$ as the solvent and tetramethylsilane as internal standard unless otherwise stated. ^{1}H NMR data of the unassigned signals are not listed. Melting points were determined in a paraffin oil bath and are uncorrected.

Phenyl 6-*O*-*tert*-butyldiphenylsilyl-1-thio-β-D-galactopyranoside (2). To a solution of phenyl 1-thio-β-D-galactopyranoside (**1**) (2.7 g, 9.9 mmol) in pyridine (16 mL), *tert*-butyldiphenylsilyl chloride (3.8 mL, 14.9 mmol) was added. The reaction mixture was stirred for 3 h at 25°C, and then concentrated under reduced pressure. Column chromatography of the residue in 1:1 toluene-EtOAc gave **2** (3.6 g, 73%) as an amorphous solid, $R_f = 0.5$, $[\alpha]_D^{25}$ − 13.8 (*c* 1.0, $CHCl_3$). ^{1}H NMR: δ 7.75–7.26 (m, 15H, aromatic protons), 4.53 (d, 1H, J = 9.6 Hz, H-1), 4.14 (d, 1H, $J_{3,4}$ = 2.4 Hz, H-4), 3.96 (m, 2H, H-6), 3.72 (t, 1H, J = 9.1 Hz, H-2), 3.05, 2.83 (2 bs, 3H, 3 O*H*), 1.08 (s, 9H, $[Ph_2SiC(CH_3)_3]$.

Anal. Calcd for $C_{28}H_{34}O_5SiS$: C, 65.84; H, 6.71. Found: C, 65.72; H, 6.69.

Phenyl 6-*O*-*tert*-butyldiphenylsilyl-3,4-*O*-isopropylidene-1-thio-β-D-galactopyranoside (3). To a solution of **2** (5 g, 9.8 mmol) in DMF (25 mL), 2,2-dimethoxypropane (1.80 mL, 14.6 mmol) and 10-camphorsulfonic acid (100 mg) were added. The mixture was stirred at room temperature for 12 h. The reaction was quenched with Et_3N, concentrated to a syrup which upon column chromatography (3:1 toluene-EtOAc), gave **3** (4.2 g, 77.9%) as a foam, $R_f = 0.82$, $[\alpha]_D^{25}$ + 7.4 (*c* 0.7, $CHCl_3$). ^{1}H NMR: δ 7.63–7.14 (m, 15H, aromatic protons), 4.37 (d, 1H, $J_{1,2}$ = 10.2 Hz, H-1), 4.18 (dd, 1H, $J_{2,3}$ = 5.4 Hz, $J_{3,4}$ = 1.3 Hz, H-3), 3.99 (t, 1H, J = 6.7 Hz, H-5), 3.93–3.80 (m, 3H, H-4,H-6), 3.48 (dd, 1H, $J_{2,3}$ = 7.1 Hz, $J_{1,2}$ = 10.1 Hz, H-2), 2.72 (bs, 1H, O*H*), 1.32, 1.24 (2s, 6H, $C(CH_3)_2$, 0.98 [s, 9H, $(CH_3)_3CSiPh_2$]. ^{13}C NMR: δ 136.1–128.1 (aromatic carbons), 110.6 [$C(CH_3)_2$], 88.6 (C-1), 79.5, 78.3, 77.1, 75.4, 73.7, 63.4 (C-6), 28.6, 26.8 [$C(CH_3)_3$], 27.2 [$Ph_2SiC(CH_3)_3$], 19.6 [$Ph_2SiC(CH_3)_3$].

Anal. Calcd for $C_{31}H_{38}O_5SiS$: C, 67.60; H, 6.95. Found: C, 67.82; H, 7.12.

Phenyl 2-*O*-acetyl-6-*O*-*tert*-butyldiphenylsilyl-3,4-*O*-isopropylidene-1-thio-β-D-galactopyranoside (4). To a solution of **3** (4 g, 7.26 mmol) in pyridine (8 mL), acetic anhydride (5 mL) was added and the mixture was stirred for 3 h. The reaction mixture was concentrated under vacuum and co-evaporated twice with toluene. Column chromatography of the syrupy material with 5:1 toluene-EtOAc gave **4** (4 g, 93%), $R_f = 0.80$, $[\alpha]_D^{25}$ + 30.3 (*c* 2.2, $CHCl_3$). ^{1}H NMR: δ 7.71–7.21 (m, 15H, aromatic protons), 5.04 (dd, 1H, $J_{2,3}$ = 7.3 Hz, $J_{1,2}$ = 10.2 Hz, H-2), 4.61 (d, 1H, J = 10.3 Hz, H-1), 4.28 (dd, 1H, $J_{3,4}$ = 5.1 Hz, $J_{4,5}$ = 1.3 Hz, H-4), 4.17 (dd, 1H, $J_{2,3}$ = 7.1 Hz, $J_{3,4}$ = 5.5 Hz, H-3), 3.93 (m, 1H, H-5), 2.11 (s, 3H, $OCOCH_3$), 1.50, 1.32 [2 s, 6H, $C(CH_3)_2$], 1.06 [s, 9H, $Ph_2SiC(CH_3)_3$]; ^{13}C NMR: δ 169.8 ($OCOCH_3$), 135.7–125.4 (aromatic carbons), 110.6 [$C(CH_3)_2$], 86.2 (C-1), 77.3, 77.1, 73.5, 71.6, 63.0 (C-6), 27.8, 21.6 [$C(CH_3)_3$], 26.9 [$Ph_2SiC(CH_3)_3$], 21.2 ($OCOCH_3$), 19.3 [$Ph_2SiC(CH_3)_3$].

Anal. Calcd for $C_{33}H_{40}O_6SiS$: C, 66.85; H, 6.80. Found: C, 66.67; H, 6.92.

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

Phenyl 2-*O*-acetyl-6-*O*-*tert*-butyldiphenylsilyl-1-thio-β-D-galactopyranoside (5). A solution of **4** (2 g, 3.37 mmol) in 80% acetic acid (20mL) was stirred at 80°C. After 1 h when TLC showed complete conversion, solvents were evaporated off. Column chromatography with 3:1 toluene-EtOAc gave **5** (1.71 g, 92%) as a foamy product, $R_f = 0.64$, $[\alpha]_D^{25}$ + 13.6 (*c* 3.3, $CHCl_3$). ^1H NMR: δ 7.65–7.01 (m, 15H, aromatic protons), 4.97 (t, 1H, J = 9.7 Hz, H-2), 4.54 (d, 1H, J = 10.0 Hz, H-1), 4.04 (d, 1H, J = 2.0 Hz, H-4), 3.88, 3.87 (2 bs, 2H, H-6), 3.54 (d, 1H, J = 7.6 Hz, H-3), 3.47 (t, 1H, J = 5.0 Hz, H-5), 3.03, 2.85 (2 bs, 1H, 3-O*H*, 4-O*H*), 2.06 (s, 3H, OCOC*H*$_3$), 0.99 [s, 9H, $Ph_2SiC(CH_3)_3$]; ^{13}C NMR: δ 171.34 (O*C*OCH$_3$), 136.1–125.7 (aromatic carbons), 86.6 (C-1), 78.3, 74.3, 71.5, 70.3, 64.3 (C-6), 27.2 [$Ph_2SiC(CH_3)_3$], 21.5 (OCO*C*H$_3$), 19.6 [$Ph_2SiC(CH_3)_3$].

Anal. Calcd for $C_{30}H_{36}O_6SiS$: C, 65.18; H, 6.56. Found: C, 64.95; H, 6.78.

Phenyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1 → 3)-2-*O*-acetyl-6-*O*-*tert*-butyldiphenylsilyl-1-thio-β-D-galactopyranoside (7). To a solution of **5** (1.07 g, 1.94 mmol) in CH_2Cl_2 (10 mL) was added 4 Å molecular sieve (2.5 g) and stirred for 2 h under N_2 at −30°C. To this solution was added TESOTf (80 µL, 0.35 mmol) and 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranose trichloroacetimidate (**6**) (1.35 g, 2.32 mmol) and the reaction mixture was allowed to stir for 30 min at that temperature. The mixture was then diluted with CH_2Cl_2 (25 mL), filtered and the filtrate washed successively with saturated $NaHCO_3$ solution and water, dried (Na_2SO_4) and concentrated. Column chromatography of the resulting syrup with 10:1 toluene-EtOAc gave **7** (1.33 g, 71%) as a white amorphous solid, $R_f = 0.70$, $[\alpha]_D^{25}$ + 18.8 (*c* 2.0, $CHCl_3$). ^1H NMR: δ 7.84–7.73 [m, 4H, $N(CO)_2C_6H_4$], 7.72–7.16 (m, 15H, aromatic protons), 5.75 (t, 1H, J = 9.2 Hz, H-3^D), 5.54 (d, 1H, J = 8.4 Hz, H-1^D), 5.15 (t, 1H, J = 9.6 Hz, H-4^D), 5.09 (t, 1H, J = 9.7 Hz, H-2^C), 4.53 (d, 1H, J = 10.1 Hz, H-1^C), 4.36 (dd, 1H, $J_{1,2}$ = 8.5 Hz, $J_{2,3}$ = 10.7 Hz, H-2^D), 4.14 (bs, 1H, H-4^C), 3.97–3.85 (m, 3H, H-5^D, H-6^C), 3.72 (dd, 1H, H-5^C), 2.66 (bs, 1H, 4-O*H*), 2.02, 1.99, 1.84, 1.57 (4 s, 12 H, OCOC*H*$_3$), 1.05 [s, 9H, $Ph_2SiC(CH_3)_3$]; ^{13}C NMR: δ 171.0, 170.6, 169.8, 169.5 (4 *C*OCH$_3$), 136.1–127.8 (aromatic carbons), 98.8 (C-1^D), 87.3 (C-1^C), 82.1, 79.1, 78.3, 72.5, 70.8, 69.1, 68.7, 63.5, 62.2 (C-6^C, C-6^D), 54.8 (C-2^D), 27.2 [$Ph_2SiC(CH_3)_3$], 21.1, 21.0, 20.8, 20.7 (4 CO*C*H$_3$), 19.6 [$Ph_2SiC(CH_3)_3$].

Anal. Calcd for $C_{50}H_{55}O_{15}SiNS$: C, 61.90; H, 5.71; N, 1.44. Found: C, 61.65; H, 5.78; N, 1.45.

Phenyl 3,4,6 tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1 → 3)-2-*O*-acetyl-1-thio-β-D-galactopyranoside (8). Tetrabutylammonium fluoride (75.3 mg, 0.29 mmol) in THF (0.2 mL) was added to a solution of **7** (380 mg, 0.39 mmol) in THF (1 mL) at 0°C, then the temperature was slowly raised to 25°C. After 6 h, the solution was concentrated. Column chromatography of the residue with 1:1 toluene-EtOAc gave **8** (202 mg, 74%), $R_f = 0.26$, $[\alpha]_D^{25}$ + 26.3 (*c* 2.4, $CHCl_3$). ^1H NMR: δ 7.85–7.72 [m, 4H, $N(CO)_2C_6H_4$], 7.40–7.14 (m, 5H, aromatic protons), 5.72 (t, 1H, J = 9.2 Hz, H-3^D), 5.56 (d, 1H, J = 8.0 Hz, H-1^D), 5.12 (t, 1H, J = 9.6 Hz, H-4^D), 5.07 (t, 1H, J = 9.4 Hz, H-2^C), 4.57 (d, 1H, J = 9.9 Hz, H-1^C), 4.25 (bs, 1H, H-4^C), 4.32–4.17 (m, 2H, H-6^D), 3.90 (m, 2H, H-6^C), 3.76 (m, 1H, H-5^D), 3.58 (t, 1H, J = 5.7 Hz, H-5^C), 2.09, 2.02, 1.84, 1.50 (4 s, 12 H, OCOC*H*$_3$); ^{13}C NMR: δ 170.8, 170.2, 169.4, 169.1 (4 *C*OCH$_3$), 134.5–123.8 (aromatic carbons), 98.4 (C-1^D), 86.5 (C-1^C), 81.7, 78.3, 72.1, 70.4, 68.9, 68.5, 62.1, 61.9 (C-6^C, C-6^D), 54.4 (C-2^D), 20.8, 20.6, 20.4, 20.2 (4 COCH_3).

Anal. Calcd for $C_{34}H_{37}O_{15}NS$: C, 58.36; H, 5.32; N, 2.00. Found: C, 58.03; H, 5.50; N, 1.90.

Phenyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1 → 3)-2-*O*-acetyl-4,6-*O*-benzylidene-1-thio-β-D-galactopyranoside (9). To a solution of **8** (200 mg, 0.29 mmol) in dry acetonitrile (1.5 mL) were added at room temperature benzaldehyde dimethylacetal (51.5 μL, 0.34 mmol) and 10-camphorsulfonic acid (30 mg) and the mixture was allowed to stir for 2 h. The reaction was quenched with Et_3N, and solvents were evaporated under reduced pressure. Column chromatography of the syrupy product with 3:1 toluene-EtOAc gave **9** (206.2 mg, 88%) as a glassy material, $R_f = 0.55$, $[\alpha]_D^{25}$ − 19.5 (*c* 1.0, $CHCl_3$). ^{1}H NMR: δ 7.83–7.70 [m, 4H, $N(CO)_2C_6H_4$], 7.49–7.16 (m, 10H, aromatic protons), 5.70 (dd, 1H, $J_{2,3}$ = 9.2 Hz, $J_{3,4}$ = 10.7 Hz, H-3^D), 5.57 (d, 1H, J = 8.4 Hz, H-1^D), 5.51 (s, 1H, PhC*H*), 5.17 (t, 1H, J = 9.7 Hz, H-4^D), 5.11 (t, 1H, J = 9.7 Hz, H-2^C), 4.55 (d, 1H, J = 9.8 Hz, H-1^C), 4.35 (m, 2H, H-6^D), 4.39 (d, 1H, J = 2.2 Hz, H-4^C), 3.85 (m, 2H, H-6^C), 3.47 (bs, 1H, H-5^C), 2.09, 2.03, 1.82, 1.69 (4 s, 12 H, OCOCH_3); ^{13}C NMR: δ 170.6, 170.2, 169.4, 168.9 (4 *C*OCH$_3$), 137.7–123.6 (aromatic carbons), 100.9 (*C*HPh), 99.0 (C-1^D), 85.8 (C-1^C), 79.4, 75.7, 72.0, 70.6, 70.1, 69.0, 68.8, 68.1 (C-6^C), 61.7 (C-6^D), 54.4 (C-2^D), 20.9, 20.6, 20.6, 20.4 (4 COCH_3).

Anal. Calcd for $C_{41}H_{41}O_{15}NS$: C, 60.06; H, 5.04; N, 1.70. Found: C, 60.26; H, 5.12; N, 1.61.

Phenyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl-(1 → 3)-2-*O*-acetyl-4,6-*O*-benzylidene-1-thio-β-D-galactopyranoside (10). To compound **9** (180 mg, 0.22 mmol) dissolved in *n*-butanol (5 mL) was added to ethylenediamine (1 mL) under N_2 atmosphere. The solution was stirred at 90°C for 20 h. Solvents were removed under reduced pressure by co-evaporation twice with toluene to give a yellow syrup. Acetic anhydride (2 mL) and pyridine (2 mL) were then added and stirring was continued at rt. After 14 h, the solution was concentrated to a syrup, which was purified by column chromatography using 1:1 toluene-EtOAc to give **10** (143 mg, 89%) as a thick glass, $R_f = 0.21$, $[\alpha]_D^{25}$ − 1.5 (*c* 1.1, $CHCl_3$). ^{1}H NMR: δ 7.60–7.15 (m, 10H, aromatic protons), 5.73 (t, 1H, $J_{2,3} = J_{3,4}$ = 9.9 Hz, H-3^D), 5.70 (bs, 1H, N*H*COCH$_3$), 5.48 (s, 1H, PhC*H*), 5.28 (d, 1H, J = 8.1 Hz, H-1^D), 5.23 (t, 1H, $J_{3,4} = J_{4,5}$ = 9.7 Hz, H-4^D), 4.97 (t, 1H, $J_{1,2} = J_{2,3}$ = 9.8 Hz, H-2^C), 4.58 (d, 1H, J = 9.8 Hz, H-1^C), 4.26 (bs, 1H, H-4^C), 4.21 (m, 2H, H-6^D), 3.12 (m, 1H, H-5^C), 2.35 (s, 3H, N*H*COCH$_3$), 2.13, 2.07, 2.01, 1.98 (4 s, 12 H, OCOCH_3); ^{13}C NMR: δ 170.9 (NH*C*OCH$_3$), 170.6, 170.0, 169.7, 169.7 (4 *C*OCH$_3$), 137.9–125.3 (aromatic carbons), 101.3 (*C*HPh), 99.6 (C-1^D), 85.4 (C-1^C), 78.2, 76.0, 71.7, 70.6, 70.1, 69.2, 69.1, 68.2(C-6^C), 62.0 (C-6^D), 56.9 (C-2^D), 23.3 (NHCOCH_3), 21.3, 20.9, 20.7, 20.6 (4 COCH_3).

Anal. Calcd for $C_{35}H_{41}O_{14}NS$: C, 57.44; H, 5.64; N, 1.91. Found: C, 57.60; H, 5.81; N, 1.77.

Phenyl 2-acetamido-3,4,6-tri-*O*-benzoyl-2-deoxy-β-D-glucopyranosyl-(1 → 3)-2-*O*-benzoyl-4,6-*O*-benzylidene-1-thio-β-D-galactopyranoside (11). To a solution of **10** (140 mg, 0.19 mmol) in dry methanol (4.5 mL), 0.5M methanolic NaOMe (0.5 mL)

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

was added. After 1 h at 25°C, the solution was neutralized with Dowex 50 (H^+) resin, filtered and the filtrate was concentrated to dryness to give the de-*O*-acetylated product in quantitative yield. To a stirred solution of the product in pyridine (800 μL), benzoyl chloride (110 μL, 0.95 mmol) was added at 0°C and the mixture was allowed to stir for 4 h. Excess benzoyl chloride was then decomposed by the addition of water (1 mL). Stirring was continued for another 30 min. The mixture was then concentrated under vacuum to a small volume, diluted with CH_2Cl_2, washed successively with a saturated aq $NaHCO_3$ solution and water. The organic layer was collected, dried (Na_2SO_4) and concentrated. Column chromatography of the residue with 5:1 toluene-EtOAc gave pure **11** (145.5 mg, 93%) as a thick glass, $R_f = 0.85$, $[\alpha]_D^{25}$ + 1.3 (*c* 0.8, $CHCl_3$). ^1H NMR: δ 8.14–7.19 (m, 30H, aromatic protons), 6.10 (t, 1H, $J_{2,3} = J_{3,4} = 9.8$ Hz, H-3^D), 5.56 (d, 1H, J = 7.3 Hz, H-1^D), 5.48 (t, 1H, J = 9.8 Hz, H-4^D), 5.46 (t, 1H, J = 8.0 Hz, H-2^C), 5.38 (s, 1H, PhC*H*), 4.73 (d, 1H, J = 9.8 Hz, H-1^C), 4.41 (d, 1H, J = 3.1 Hz, H-4^C), 4.11 (m, 1H, H-5^D), 2.35 (s, 3H, N*H*$COCH_3$); ^{13}C NMR: δ 171.8 (NH*C*OCH_3), 166.0, 165.7, 165.3, 165.0 (4 *C*OC_6H_5), 133.8–126.7 (aromatic carbons), 101.1 (*C*HPh), 100.8 (C-1^D), 85.3 (C-1^C), 80.4, 75.9, 71.9, 71.2, 70.2, 69.8, 68.9, 68.5 (C-6^C), 62.5 (C-6^D), 56.9 (C-2^D), 22.3 (NHCO*C*H_3).

Anal. Calcd for $C_{55}H_{49}O_{14}NS$: C, 67.40; H, 5.03; N, 1.42. Found: C, 67.27; H, 5.27; N, 1.37.

Phenyl 2-acetamido-3,4,6-tri-*O*-benzoyl-2-deoxy-β-D-glucopyranosyl-(1 → 3)-2-*O*-benzoyl-1-thio-β-D-galactopyranoside (12). A solution of **11** (105 mg, 0.11 mmol) in 80% acetic acid (1.05 mL) was heated at 70°C for 1 h. Solvents were evaporated off. Column chromatography of the residue with 2:1 toluene-EtOAc gave **12** (77.4 mg, 81%), $R_f = 0.44$, $[\alpha]_D^{25}$ − 1.0 (*c* 1.5, $CHCl_3$). ^1H NMR: δ 7.99–7.15 (m, 25H, aromatic protons), 5.77 (d, 1H, J = 8.9 Hz, N*H*$COCH_3$), 5.76 (t, 1H, J = 10.8 Hz, H-3^D), 5.45 (t, 1H, J = 9.9 Hz, H-4^D), 5.41 (t, 1H, J = 9.7 Hz, H-2^C), 5.20 (d, 1H, J = 8.1 Hz, H-1^D), 4.79 (d, 1H, J = 10.1 Hz, H-1^C), 4.58 (dd, 1H, $J_{2,3} = 12.3$ Hz, $J_{3,4} = 2.7$ Hz, H-3^C), 4.24 (d, 1H, J = 2.7 Hz, H-4^C), 4.05 (m, 1H, H-5^D), 3.84 (m, 1H, H-5^C), 1.13 (s, 3H, N*H*$COCH_3$); ^{13}C NMR: δ 171.5 (NH*C*OCH_3), 166.6, 166.5, 165.7, 165.6 (4 *C*OC_6H_5), 133.9–128.2 (aromatic carbons), 101.3 (C-1^D), 87.0 (C-1^C), 82.6, 78.4, 72.5, 72.1, 70.1, 69.9, 69.3, 63.1, 62.8 (C-6^C, C-6^D), 56.3 (C-2^D), 22.7 (NHCO*C*H_3).

Anal. Calcd for $C_{48}H_{45}O_{14}NS$: C, 64.63; H, 5.08; N, 1.57. Found: C, 64.50; H, 4.90; N, 1.40.

Phenyl 2-acetamido-3,4,6-tri-*O*-benzoyl-2-deoxy-β-D-glucopyranosyl-(1 → 3)-2-*O*-benzoyl-4,6-*O*-[(R)-1-methoxycarbonylethylidene]-1-thio-β-D-galactopyranoside (13). To a solution **12** (100 mg, 0.11 mmol) in acetonitrile (0.3 mL), $BF_3 \cdot OEt_2$ (28.4 μL, 0.22 mmol) and methyl pyruvate (20.3 μL, 0.22 mmol) were added, and the mixture was stirred under N_2 for 3 h at room temperature. The reaction mixture was then diluted with CH_2Cl_2 and poured into an aq $NaHCO_3$ solution. The organic layer was separated and the aqueous layer was extracted twice with CH_2Cl_2. Concentration of the combined organic layers gave a foamy product which on chromatography with 1:1 toluene-EtOAc afforded **13** (47.6 mg, 45%), $R_f = 0.72$, $[\alpha]_D^{25}$ − 30.8 (*c* 0.5, $CHCl_3$) together with 25 mg of the corresponding (*R*) and (*S*) mixture. ^1H NMR of **13**: δ 8.00–7.20 (m, 25H, aromatic protons), 5.82 (t, 1H, J = 9.9 Hz, H-3^D), 5.75 (d, 1H, J = 8.3 Hz, N*H*$COCH_3$), 5.41 (t, 1H, J = 9.7 Hz, H-4^D), 5.38 (t, 1H, J = 9.4 Hz, H-2^C), 5.27 (d, 1H, J = 8.2 Hz,

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

H-1^{D}), 4.63 (d, 1H, J = 9.7 Hz, H-1^{C}), 4.32 (d, 1H, J = 2.7 Hz, H-4^{C}), 4.08 (m, 1H, H-5^{D}), 3.72 (s, 3H, COOC*H*$_3$), 1.47 (s, 3H, NHCOC*H*$_3$), 1.22 [s, 3H, C(C*H*$_3$)COOCH$_3$]; ^{13}C NMR: δ 170.1 (NH*C*OCH$_3$),169.1 (*C*OOCH$_3$) 164.9, 164.8, 164.3, 164.1 (4 *C*OC$_6$H$_5$), 135.7–127.0 (aromatic carbons), 100.3 [*C*(CH$_3$)COOCH$_3$], 97.4 (C-1^{D}), 84.7 (C-1^{C}), 79.3, 71.1, 71.0, 70.8, 70.3, 69.1, 68.1, 67.1, 67.0, 64.2, 62.5 (C-6^{C}, C-6^{D}), 54.8 (C-2^{D}), 51.6 (COO*C*H$_3$), 25.8 [C(*C*H$_3$)COOCH$_3$], 22.5 (NHCO*C*H$_3$).

Anal. Calcd for $C_{52}H_{49}O_{16}NS$: C, 63.99; H, 5.06; N, 1.43. Found: C, 63.80; H, 5.28; N, 1.56.

2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-α,β-D-mannopyranose (15). To a stirred solution of ethyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-1-thio-α-D-mannopyranoside (**14**) (1.1 g, 2.23 mmol) in CH_2Cl_2 (14.38 mL), water (360 μL) and $(CF_3CO_2)_2Hg$ (1.04 g, 2.45 mmol) were added at 0°C. The mixture was stirred at rt for 12 h. The contents were then diluted with CH_2Cl_2 and filtered through a Celite bed. The organic layer was washed successively with water, 5% KI solution and water, dried (Na_2SO_4) and concentrated. Column chromatography with 3:1 toluene:EtOAc gave **15** (715 mg, 71 %), R_f = 0.62, $[\alpha]_D^{25}$ − 9.2 (*c* 0.6, CHCl$_3$). ^{1}H NMR : δ 7.54–7.25 (m, 15H, aromatic protons), 5.65 (s, 1H, C*H*C$_6$H$_5$).

Anal. Calcd for $C_{27}H_{28}O_6$: C, 72.30; H, 6.29. Found: C, 72.05; H, 6.19.

2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-α,β-D-mannopyranosyl trichloroacetimidate (16). To a solution of **15** (700 mg, 1.56 mmol) in CH_2Cl_2 (7 mL) was added K_2CO_3 (775 mg) and trichloroacetonitrile (782 μL) and the mixture was vigorously stirred for 5 h at room temperature under N_2. The mixture was filtered through a Celite bed, washed with CH_2Cl_2, dried (Na_2SO_4), and concentrated to a syrup. Column chromatography with 1:1 petroleum ether (60–80°C)-EtOAc (containing 0.1% triethylamine) gave **16** (675 mg, 73%) as a foam, R_f = 0.90, $[\alpha]_D^{25}$ + 72.5 (*c* 1.5, CHCl$_3$). ^{1}H NMR (α-isomer): δ 8.67 [s, 1H, OCN*H*CCl$_3$], 7.51–7.25 (m, 15H, aromatic protons), 5.83 (s, 1H, H-1), 5.62 (s, 1H, C*H*C$_6$H$_5$), 3.52 (m, 1H, H-5); ^{1}H NMR (β-isomer): 8.57 [s, 1H, OCN*H*CCl$_3$], 7.51–7.25 (m, 15H, aromatic protons), 6.26 (s, 1H, H-1), 5.66 (s, 1H, C*H*C$_6$H$_5$), 3.52 (m, 1H, H-5).

Anal. Calcd for $C_{29}H_{28}O_6NC_{l3}$: C, 58.74; H, 4.75; N, 2.36. Found: C, 58.56; H, 4.97; N, 2.18.

2-(Trimethylsilyl)ethyl 3,4-*O*-isopropylidene-β-D-galactopyranoside (17). To a solution of 2-(trimethylsilyl)ethyl β-D-galactopyranoside[24] (3.8 g, 13.6 mmol) in DMF (3mL), 2,2-dimethoxypropane (2.5 mL, 20.3 mmol) was added followed by the addition of 10-camphorsulfonic acid (100 mg). The reaction was conducted as described for compound **3** and monitored by TLC (3:1 toluene-EtOAc), giving **17** (2.7 g, 63.8%) as a syrup, R_f = 0.46, $[\alpha]_D^{25}$ + 5.3 (*c* 3.8, CHCl$_3$). ^{1}H NMR: δ 4.03 (d, 1H, J = 8.3 Hz, H-1), 3.99 (dd, 1H, $J_{2,3}$ = 5.6 Hz, $J_{3,4}$ = 1.8 Hz, H-3), 3.69 [m, 2H, OC*H*$_2$CH$_2$Si(CH$_3$)$_3$], 3.45–3.31 (m, 2H, H-5, H-6), 2.62, 2.25 (2 bs, 2H, 2-O*H*, 6-O*H*), 1.34, 1.17 [2 s, 6H, C(C*H*$_3$)$_2$], 0.83 [m, 2H, OCH$_2$C*H*$_2$Si(CH$_3$)$_3$], − 0.15 [s, 9H, OCH$_2$CH$_2$Si(C*H*$_3$)$_3$]. ^{13}C NMR: δ 110.8 [*C*(CH$_3$)$_2$], 102.2 (C-1), 79.3, 74.3, 74.0, 73.8, 67.7 [O*C*H$_2$CH$_2$Si(CH$_3$)$_3$], 62.7 (C-6), 28.5, 26.8 [C(*C*H$_3$)$_2$], 18.7 [OCH$_2$*C*H$_2$Si(CH$_3$)$_3$], − 1.0 [OCH$_2$CH$_2$Si(*C*H$_3$)$_3$].

Anal. Calcd for $C_{14}H_{28}O_6Si$: C, 52.47; H, 8.80. Found: C, 52.65; H, 8.61.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

2-(Trimethylsilyl)ethyl 2,6-di-*O*-benzyl-3,4-*O*-isopropylidene-β-D-galactopyranoside (18). To a cold solution of **17** (2.5 g, 7.8 mmol) in DMF (10 mL), NaH (1.87 g, 39.0 mmol) and benzyl bromide (2.8 mL, 23.4 mmol) were added. The mixture was stirred at room temperature for 3 h. The reaction was quenched with MeOH, diluted with water and repeatedly extracted with ether. The organic layer was washed with water, dried (Na_2SO_4), and concentrated. Column chromatography with 8:1 toluene-EtOAc gave **18** (3.38 g, 86.7%) as a thick syrup, $R_f = 0.71$, $[\alpha]_D^{25} + 18.5$ (*c* 2.7, $CHCl_3$). ^{1}H NMR: δ 7.24–7.05 (m, 10H, aromatic protons), 4.69 (2d, 2H, J = 11.8 Hz, CH_2Ph), 4.46 (2d, 2H, J = 11.8 Hz, CH_2Ph), 4.12 (d, 1H, J = 8.0 Hz, H-1), 3.24 (m, 1H, H-5), 1.21, 1.18 [2s, 6H, C(CH_3)$_2$], 0.90 (t, 2H, J = 8.4 Hz, OCH$_2$CH_2SiMe$_3$), −0.15 [s, 9H, OCH$_2$CH$_2$Si(CH_3)$_3$]. ^{13}C NMR: δ 138.8–127.9 (aromatic carbons), 110.3 [*C*(CH$_3$)$_2$], 102.8 (C-1), 80.2, 79.5, 74.3, 74.1, 74.0, 72.6, 70.1 (O*C*H$_2$CH$_2$SiMe$_3$), 67.6 (C-6), 28.2, 26.8 [C(*C*H$_3$)$_2$], 18.9 (OCH$_2$*C*H$_2$SiMe$_3$), −1.5 [OCH$_2$CH$_2$Si(*C*H$_3$)$_3$].

Anal. Calcd for $C_{28}H_{40}O_6Si$: C, 67.16; H, 8.05. Found: C, 67.30; H, 7.88.

2-(Trimethylsilyl)ethyl 2,6-di-*O*-benzyl-β-D-galactopyranoside (19). A solution of **18** (2.4 g, 4.79 mmol) in 80% aq acetic acid (24 mL) was heated at 80°C for 1 h. Solvents were then evaporated off. Column chromatography with 3:1 toluene-EtOAc gave **19** (2.04 g, 92.8%) as a syrup, $R_f = 0.42$, $[\alpha]_D^{25} + 5.2$ (*c* 3.0, $CHCl_3$). ^{1}H NMR: δ 7.31–7.18 (m, 10H, aromatic protons), 4.89, 4.62 (2d, 2H, J = 11.5 Hz, CH_2Ph), 4.49 (s, 2H, CH_2Ph), 4.29 (d, 1H, J = 7.3 Hz, H-1), 3.94 (dd, 1H, $J_{1,2}$ = 7.0 Hz, $J_{2,3}$ = 10.7 Hz, H-2), 3.83 (d, 1H, J = 2.4 Hz, H-4), 3.67 [m, 2H, OCH_2CH$_2$Si(CH$_3$)$_3$], 2.89 (bs, 2H, 3-O*H*, 4-O*H*), 0.96 [m, 2H, OCH$_2$CH_2Si(CH$_3$)$_3$], −0.04 [s, 9H, OCH$_2$CH$_2$Si(CH_3)$_3$]. ^{13}C NMR: δ 138.6–127.5 (aromatic carbons), 110.0 (*C*Me$_2$), 103.1 (C-1), 79.3, 74.5, 73.5, 73.3, 73.2, 69.4, 69.0 (2*C*H$_2$Ph), 67.3 (C-6), 18.5 [OCH$_2$*C*H$_2$Si(CH$_3$)$_3$], −1.5 [OCH$_2$CH$_2$Si(*C*H$_3$)$_3$].

Anal. Calcd for $C_{25}H_{36}O_6Si$: C, 65.18; H, 7.87. Found: C, 65.02; H, 7.65.

2-(Trimethylsilyl)ethyl 2,6-di-*O*-benzyl-3-*O*-(4-methoxybenzyl)-β-D-galactopyranoside (20). To a solution of **19** (1.1 g, 2.38 mmol) in benzene (50 mL), and Bu_2SnO (653 mg, 2.6 mmol) was added and the mixture was refluxed for 8 h in a Dean-Stark apparatus. The solution was cooled, 4-methoxybenzyl chloride (387 μL, 2.86 mmol) and Bu_4NBr (920 mg, 2.86 mmol) were added, and the reaction was allowed to continue at 63°C for 6 h. The benzene solution was concentrated, MeOH was added and the mixture was kept at −5°C for 2 h. The tin compound precipitated out and filtered off. The filtrate was concentrated and the syrupy product was purified by column chromatography with 4:1 toluene-EtOAc to afford **20** (1.02 g, 74.5%) as a glass, $R_f = 0.65$, $[\alpha]_D^{25} - 1.1$ (*c* 1.7, $CHCl_3$). ^{1}H NMR: δ 7.22–7.09 (m, 10H, aromatic protons), 7.07, 6.65 (2 d, 4H, J = 6.7 Hz, CH$_2$C$_6$*H*$_4$OCH$_3$), 4.72, 4.53 (2d, 2H, J = 11.0 Hz, CH_2Ph), 4.46 (s, 2H, CH_2C$_6$H$_4$OCH$_3$), 4.38 (s, 2H, CH_2Ph), 4.16 (d, 1H, J = 7.7 Hz, H-1), 3.78 (d, 1H, J = 3.4 Hz, H-4), 3.58 [s, 3H, CH$_2$C$_6$H$_4$OCH_3), 3.65–3.51 [m, 2H, OCH_2CH$_2$Si(CH$_3$)$_3$], 3.38 (m, 3H, H-5, H-6), 0.87 [t, 2H, J = 8.4 Hz, OCH$_2$CH_2Si(CH$_3$)$_3$], −0.15 [s, 9H, OCH$_2$CH$_2$Si(CH_3)$_3$]; ^{13}C NMR: δ 159.3–113.8 (aromatic carbons), 103.1 (C-1), 80.2, 79.0, 75.1, 73.6, 73.1, 71.9, 69.2, 67.2 (*C*H$_2$Ph), 66.8 (C-6), 55.2 (CH$_2$C$_6$H$_4$O*C*H$_3$), 18.4 [OCH$_2$*C*H$_2$Si(CH$_3$)$_3$], −1.5 [OCH$_2$CH$_2$-Si(*C*H$_3$)$_3$].

Anal. Calcd for $C_{33}H_{44}O_7Si$: C, 68.24; H, 7.63. Found: C, 68.10; H, 7.59.

2-(Trimethylsilyl)ethyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-mannopyranosyl-(1 → 4)-2,6-di-*O*-benzyl-3-*O*-(4-methoxybenzyl)-β-D-galactopyranoside (21). To a solution of the acceptor **20** (180 mg, 0.31 mmol) in CH_2Cl_2 (1.6 mL) was added 4 Å molecular sieves (300 mg) and the suspension stirred for 2 h at −30°C. To this mixture was added TESOTf (12.6 μL, 0.06 mmol) and the trichloroacetimidate donor **16** (220 mg, 0.73 mmol) and the solution was allowed for stir for 30 min at that temperature. The reaction mixture was then diluted with CH_2Cl_2 (25 mL) and washed successively with saturated $NaHCO_3$ and water. The organic phase was collected, dried (Na_2SO_4) and concentrated to a syrup. Column chromatography of the residue with 10:1 toluene-EtOAc gave pure disaccharide **21** (223 mg, 70%), $R_f = 0.66$, $[\alpha]_D^{25} -23.5$ (*c* 2.0, $CHCl_3$) together with 45 mg (14%) of the corresponding α anomer (**21a**), $[\alpha]_D^{25}$ + 126.5 (*c* 0.7, $CHCl_3$). ^1H NMR of **21**: δ 7.33–7.05 (m, 25H, aromatic protons), 6.97, 6.61 (2d, 4H, J = 8.4 Hz, $CH_3OC_6H_4CH_2$), 5.41 (s, 1H, CHC_6H_5), 4.76 (d, 1H, J = 3.0 Hz, H-2^B), 4.78, 4.67 (2d, 2H, J = 12.4 Hz,CH_2Ph), 4.77, 4.52 (2d, 2H, J = 11.0 Hz,CH_2Ph), 4.53, 4.33 (2d, 2H, J = 11.2 Hz,CH_2Ph), 4.59 (bs, 1H, H-1^B), 4.36 (s, 2H, $CH_3OC_6H_4CH_2$), 4.21 (d, 1H, J = 7.6 Hz, H-1^A), 3.85 (dd, 1H, $J_{2,3}$ = 3.0 Hz, $J_{3,4}$ = 10.1 Hz, H-3^B) 3.54 (s, 3H, $CH_2C_6H_4OCH_3$), 3.50 [m, 2H, $OCH_2CH_2Si(CH_3)_3$], 0.88 [m, 2H, $OCH_2CH_2Si(CH_3)_3$], −0.15 [s, 9H, $OCH_2CH_2Si(CH_3)_3$]; ^{13}C NMR: δ 138.6–125.9 (aromatic carbons), 103.3 (C-1^A), 102.3 (C-1^B), 101.2 (*C*HPh), 81.5, 79.3, 78.3, 78.2, 75.1, 74.9, 74.3, 73.3, 73.3, 73.2, 73.1, 71.9, 69.4, 68.4 ($OCH_2CH_2SiMe_3$), 67.5, 67.1 (C-6^A, C-6^B), 55.1 ($CH_2C_6H_4OCH_3$), 18.4 ($OCH_2CH_2SiMe_3$), −1.5 [$OCH_2CH_2Si(CH_3)_3$]. ^1H NMR of **21a**: δ 7.35–6.62 (m, 25H, aromatic protons), 6.99, 6.63 (2d, 4H, J = 8.2 Hz, $CH_2C_6H_4OMe$), 5.45 (s, 1H, C*H*Ph), 4.68 (bs, 1H, H-1^B), 4.16 (d, J = 7.6 Hz, H-1^A), 3.59 (s, 3H, $C_6H_4OCH_3$), 0.74 (m, 2H, $OCH_2CH_2SiMe_3$), −0.18 [s, 9H, $OCH_2CH_2Si(CH_3)_3$]; ^{13}C NMR: δ 159.0, 138.2–126.0 (aromatic carbons), 103.7 (C-1^A), 101.1 (*C*HPh), 101.0 (C-1^B), 79.5, 79.2, 78.7, 77.0, 74.9, 74.3, 73.8, 73.6, 73.2, 72.6, 72.2, 72.1, 72.1, 68.8, 68.0, 64.4 (C-6^A, C-6^B), 55.1 ($CH_2C_6H_4OCH_3$), 18.5 ($OCH_2CH_2SiMe_3$), −1.5 [$OCH_2CH_2Si(CH_3)_3$].

Anal. Calcd for: $C_{60}H_{70}O_{12}Si$ (**21**): C, 71.26; H, 6.97; Found: C, 71.08; H, 7.10.

2-(Trimethylsilyl)ethyl 2,3,6-tri-*O*-benzyl-β-D-mannopyranosyl-(1 → 4)-2,6-di-*O*-benzyl-3-*O*-(4-methoxybenzyl)-β-D-galactopyranoside (22). To a vigorously stirred suspension of **21** (180 mg, 0.18 mmol) and $NfsaBH_3CN$ (100 mg, 1.60 mmol) in THF (5 mL) containing 3 Å molecular sieves (100 mg), a saturated ethereal HCl solution was added dropwise at 0°C until the solution was acidic and evolution of H_2 ceased. The solution was stirred for another 10 min, when TLC indicated almost total conversion of the starting material. The reaction mixture was diluted with CH_2Cl_2 and filtered through a Celite bed. The filtrate was washed successively with water, saturated aq $NaHCO_3$ (3 × 30 mL) and water. The organic phase was dried (Na_2SO_4), concentrated and column chromatographed with 10:1 toluene-EtOAc to give **22** (126.3 mg, 70.0%) as a thick syrup, $R_f = 0.40$, $[\alpha]_D^{25}$ − 30.3 (*c*1.3, $CHCl_3$). ^1H NMR: δ 7.38–7.03 (m, 25H, aromatic protons), 7.00, 6.62 (2d, 4H, J = 8.4 Hz, $CH_3OC_6H_4CH_2$), 4.57 (s, 1H, H-1^B), 4.59 (d, 2H, J = 11.7 Hz,CH_2Ph), 4.51 (d, 1H, J = 11.7 Hz, CH_2Ph), 4.38 (d, 1H, J = 11.8 Hz,CH_2Ph), 4.31 (d, 1H, J = 11.8 Hz,CH_2Ph), 4.32 (s, 2H $CH_3OC_6H_4CH_2$), 4.22 (d, 1H, J = 7.4 Hz, H-1^A), 3.94 (bs, 1H, H-4^A), 3.61[m, 2H, $OCH_2CH_2Si(CH_3)_3$], 3.54 (s, 3H, $CH_3OC_6H_4CH_2$), 3.15 (m, 1H, H-5^A), 3.09 (dd, 1H, J = 2.4 Hz, J = 9.4Hz, H-5^B), 2.47 [bs, 1H, 4-OH), 0.89 [m, 2H, OCH_2CH_2-

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

$Si(CH_3)_3)]$, −0.15 [s, 9H, $OCH_2CH_2Si(CH_3)_3$]; ^{13}C NMR: δ 159.4 ($CH_2C_6H_4OCH_3$), 139.0–127.4 (aromatic carbons), 103.5 (C-1^A), 102.0 (C-1^B), 81.9, 81.6, 79.6, 75.5, 75.1, 73.9, 73.8, 73.7, 73.5, 73.1, 72.7, 71.1, 70.9, 70.3 ($OCH_2CH_2SiMe_3$), 68.4, 67.4, (C-6^A, C-6^B), 55.3 ($CH_2C_6H_4OCH_3$), 18.6 [$OCH_2CH_2Si(CH_3)_3$], −1.3 [OCH_2CH_2-$Si(CH_3)_3$].

Anal. Calcd for: $C_{60}H_{72}O_{12}Si$: C, 71.11; H, 7.16. Found: C, 70.95; H, 7.34.

2-(Trimethylsilyl)ethyl 2-acetamido-3,4,6-tri-*O*-benzoyl-2-deoxy-β-D-glucopyranosyl-(1 → 3)-2-*O*-benzoyl-4,6-*O*-[(*R*)-1-methoxycarbonylethylidene]-β-D-galactopyranosyl-(1 → 4)-2,3,6-tri-*O*-benzyl-β-D-mannopyranosyl-(1 → 4)-2,6-di-*O*-benzyl-3-*O*-(4-methoxybenzyl)-β-D-galactopyranoside (23). To a solution of the donor **13** (112 mg, 0.12 mmol) and the acceptor **22** (100 mg, 0.10 mmol) in dry CH_2Cl_2 (3 mL), 4 Å molecular sieves (300 mg) was stirred under N_2 for 2 h. The mixture was then cooled to −10°C, NIS (34.5 mg, 0.15 mmol) and TfOH (1.5 μL, 0.01 mmol) were added, and the mixture was allowed to stir for 25 min at this temperature. The reaction mixture was then diluted with CH_2Cl_2 (25 mL) and filtered through a Celite bed. The filtrate was washed successively with 10% aq $Na_2S_2O_3$, saturated aq $NaHCO_3$ and water, dried (Na_2SO_4) and concentrated. Column chromatography of the resulting syrupy product with 3:1 toluene-EtOAc gave **23** (122.4 mg, 66%) as a foam, R_f = 0.63, $[\alpha]_D^{25}$ −2.5 (*c* 0.6, $CHCl_3$). ^1H NMR: δ 7.84–7.04 (m, 45H, aromatic protons), 6.95, 6.63, (2d, 4H, J = 8.4 Hz, $CH_3OC_6H_4CH_2$), 5.70 (t, 1H, J = 9.9 Hz, H-3^D), 5.14 (d, 1H, J = 8.2 Hz, H-1^C), 4.71 (bs, 1H, H-1^B), 4.56 (d, 1H, J = 7.9 Hz, H-1^A), 4.07 (d, 1H, J = 3.4 Hz, H-4^C), 3.75 (d, 1H, J = 3.3 Hz, H-4^A), 3.60 (s, 3H $CH_3OC_6H_4CH_2$), 3.55 (s, 3H, $COOCH_3$), 1.44 (s, 3H, $NHCOCH_3$), 1.10 [s, 3H, $C(CH_3)COOCH_3$], 0.89 [m, 2H, $OCH_2CH_2Si(CH_3)_3$], −0.15 [s, 9H, $OCH_2CH_2Si(CH_3)_3$]; ^{13}C NMR: δ 170.6 ($COOCH_3$), 170.2 ($NHCOCH_3$), 165.9, 165.8, 165.1, 165.0 (4 COC_6H_5), 138.8–126.6 (aromatic carbons), 103.2 (C-1^A), 101.6 (C-1^C), 101.4 (C-1^B), 100.9 [$C(CH_3)COOCH_3$], 98.3 (C-1^D), 81.1, 79.4, 78.7, 75.4, 75.2, 74.9, 73.7, 73.6, 73.2, 73.0, 72.9, 72.7, 71.9, 71.7, 71.2, 70.6, 70.3 (CH_2), 70.2, 69.9, 69.3 ($OCH_2CH_2SiMe_3$), 69.0, 67.1 (one CH_2 of C-6), 66.9, 65.4, 64.7, 63.3 (three CH_2 of C-6), 55.7 ($CH_2C_6H_4OCH_3$), 55.2 ($COOCH_3$), 52.4 (C-2^D), 25.8 [$C(CH_3)COOCH_3$], 22.3 ($NHCOCH_3$), 18.4 [OCH_2CH_2 $Si(CH_3)_3$], −1.5 [$OCH_2CH_2Si(CH_3)_3$]. DEPT (135) Spectrum of **23**: δ 103.2 (C-1^A), 101.6 (C-1^C), 101.4 (C-1^B),100.8 (C-1^D), 81.1, 79.4, 78.7, 75.5, 75.1 (5 CH carbons), 74.9 (CH_2), 73.7, 73.5 (2 CH carbons), 73.2, 73.1 (2 CH_2 carbons), 72.9, 72.8 (2 CH carbons), 72.7 (CH_2), 71.9, 71.7 (2 CH carbons), 71.1 (CH_2), 70.5 (CH), 70.3 (CH_2), 69.8, 69.7 (2 CH carbons), 69.0 ($OCH_2CH_2SiMe_3$), 67.5 (CH), 67.1 (one CH_2 of C-6), 65.4 (CH), 65.1, 64.7, 63.3 (three CH_2 of C-6), 55.7 ($CH_2C_6H_4OCH_3$), 55.1 ($COOCH_3$), 52.4 (C-2^D), 25.8 [$C(CH_3)COOCH_3$], 22.3 ($NHCOCH_3$), 18.4 [OCH_2CH_2 $Si(CH_3)_3$], −1.5 [$OCH_2CH_2Si(CH_3)_3$].

Anal. Calcd for: $C_{106}H_{115}O_{28}NSi$: C, 67.75; H, 6.16; N, 0.75. Found: C, 67.49; H, 6.02; N, 0.73.

ACKNOWLEDGMENT

Financial support from the Department of Science and Technology, New Delhi, India (Project No. SP/S1/G14/95) is thankfully acknowledged.

REFERENCES

1. Robbins, J.B.; Schneerson, R.; Czu, S.C.; Pozsgay, V. Bacterial polysaccharide-protein conjugate vaccines. Pure Appl. Chem. **1999**, *71*, 745–754.
2. Dubois, E.P.; Robbins, J.B.; Pozsgay, V. Chemical approaches to bacterial vaccines. Synthesis of mycobacterial oligosaccharide-protein conjugates for use as serodiagnostics and immunogens. Bioorg. Med. Chem. Lett. **1996**, *6*, 1387–1392.
3. Pozsgay, V.; Glaudemans, C.P.J.; Robbins, J.B.; Schneerson, R. Synthesis of a tetrasaccharide donor corresponding to the O-specific polysaccharide of *Shigella dysenteriae* type 1. Carbohydr. Res. **1993**, *244*, 259–273.
4. Pozsgay, V. Synthetic *Shigella* vaccines: a carbohydrate protein conjugate with totally synthetic hexadecasaccharide haptens. Angew. Chem. Int. Ed. **1998**, *37*, 138–142.
5. Pozsgay, V. Synthesis of a hexadecasaccharide fragment of the O-polysaccharide of *Shigella dysenteriae* type 1. J. Am. Chem. Soc. **1995**, *117*, 6673–6681.
6. Paulsen, H.; Bünsch, H. Synthese der pentasaccharid-sequenz der repeating-unit der O-spezifischen seitenkette des lipopolysaccharides von *Shigella dysenteriae*. Tetrahedron Lett. **1981**, *22*, 47–50.
7. Mulard, L.A.; Ughetto-Monfrin, J. Linear synthesis of the methyl glycosides of tri-, tetra-, and pentasaccharide fragments of the *Shigella flexneri* seroytpe 5a O-antigen. J. Carbohydr. Chem. **2000**, *19*, 503–526.
8. Costachel, C.; Sansonetti, P.J.; Mulard, L.A. Linear synthesis of the methyl glycosides of tetra- and pentasaccharide fragments specific for the *Shigella flexneri* serotype 2a O-antigen. J. Carbohydr. Chem. **2000**, *19*, 1131–1150.
9. Mukhopadhyay, B.; Roy, N. Synthesis of the pentasaccharide related to the repeating unit of the antigen from *Shigella dysenteriae* type 4 in the form of its methyl ester 2-(trimethylsilyl)ethyl glycoside. Carbohydr. Res. **2003**, *338*, 589–596.
10. Mukherjee, I.; Das, S.K.; Mukherjee, A.; Roy, N. Synthesis of the tetrasaccharide related to the repeating unit of the antigen from *Shigella dysenteriae* type 5. Carbohydr. Res. **2000**, *325*, 245–252.
11. Dmitriev, B.A.; Knirel, Y.A.; Vinogradov, E.V.; Kochetkov, N.K.; Gofman, I.L. Bacterial antigenic polysaccharides VII. Structure of the polysaccharide chain of *Shigella dysenteriae* type 9 lipopolysaccharide. Bioorg. Khim. **1978**, *4*, 40–46.
12. Pal, J.; Basu, S.; Rao, C.V.N. Immunochemical studies on *Shigella dysenteriae* Type 9 bacterial polysaccharide. Carbohydr. Res. **1983**, *114*, 123–135.
13. Janak, N.; Patil, J.R.; Bose, J.L. Synthesis of some aryl β-thioglycosides. Indian J. Chem. **1968**, *7*, 227–229.
14. Hanessian, S.; Lavallee, P. The preparation and synthetic utility of *tert*-butyldiphenylsilyl ethers. Can. J. Chem. **1975**, *53*, 2975–2977.
15. Lipták, A.; Imre, J.; Nánási, P. Preparation of carbohydrate isopropylidene derivatives with 2,2-dimethoxypropane in the presence of toluene-*p*-sulphonic acid. Carbohydr. Res. **1981**, *92*, 154–156.
16. Yang, F.; He, H.; Du, Y. Synthesis of (1 → 6)-β-D-glucosamine hexasaccharide, a potential antitumor and immunostimulating agent. Tetrahedron Lett. **2002**, *43*, 7561–7563.
17. Posgay, V.; Coxon, B.; Yeh, H. Synthesis of di- to pentasaccharides related to the

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

O-specific polysaccharide of *Shigella dysenteriae* type 1, and their nuclear magnetic resonance study. Bioorg. Med. Chem. **1993**, *1*, 237–257.
18. Evans, M.E. Methyl 4,6-*O*-benzylidene α- and β-D-glucopyranoside via acetal exchange. In *Methods in Carbohydrate Chemistry*; Whistler, R.L., BeMiller, J.N., Eds.; Academic Press: New York, 1980; Vol. 8, 313–315.
19. Kanie, O.; Crawley, S.C.; Palcic, M.M.; Hindsgaul, O. Acceptor-substrate recognition by *N*-acetylglucosaminyltransferase-V; Critical role of the 4″-hydroxyl group in β-D-Glc*p*NAc-(1 → 2)-α-D-Man*p*-(1 → 6)-β-D-Glc*p*-OR. Carbohydr. Res. **1993**, *243*, 139–164.
20. Ziegler, T.; Eckhardt, E.; Strayle, J.; Herzog, H. Synthesis of 5-aminopentyl 4,6-*O*-[(*R*)-1-carboxyethylidene]-β-D-galactopyranoside and its use as a ligand for the affinity chromatography of human serum amyloid P protein. Carbohydr. Res. **1994**, *253*, 167–183.
21. Garegg, P.J.; Jansson, P.-E.; Lindberg, B.; Lindh, F.; Lönngren, J. Configuration of the acetal carbon atom of pyruvic acid acetals in some bacterial polysaccharides. Carbohydr. Res. **1980**, *78*, 127–132.
22. Garegg, P.J.; Kvarnström, I.; Niklasson, A.; Niklasson, G.; Svensson, S.C.T. Partial substitution of thioglycosides by phase transfer catalysed benzoylation and benzylation. J. Carbohydr. Chem. **1993**, *12*, 933–953.
23. Pozsgay, V. Synthesis of glycocongugate vaccines against *Shigella dysenteriae* type 1. J. Org. Chem. **1998**, *63*, 5983–5999.
24. Weingart, R.; Schmidt, R.R. Can preferential β-mannoside formation with 4,6-*O*-benzylidene protected mannopyranosyl sulfoxide be reached with trichloroacetimidates? Tetrahedron Lett. **2000**, *41*, 8753–8758.
25. Jansson, K.; Ahlfors, S.; Frejd, T.; Kihlberg, J.; Magnusson, G. 2-(Trimethylsilyl)-ethyl glycosides. Synthesis, anomeric deblocking and transformation into 1,2-trans 1-*O*-acetyl sugars. J. Org. Chem. **1988**, *53*, 5629–5647.
26. Garegg, P.J.; Hultberg, H.; Wallin, S. A novel reductive ring-opening of carbohydrate benzylidene acetals. Carbohydr. Res. **1982**, *108*, 97–101.
27. Matsuo, I.; Isomura, M.; Ajisaka, K. Synthesis of an asperagine-linked core pentasaccharide by means of simultaneous inversion reaction. J. Carbohydr. Chem. **1999**, *18*, 841–850.
28. Veeneman, G.H.; van Leeuwen, S.H.; van Boom, J.H. Iodonium ion promoted reactions at the anomeric center. II. An efficient thioglycoside mediated approach towards the formation of 1,2-trans linked glycosides and glycosidic esters. Tetrahedron Lett. **1990**, *31*, 1331–1334.

Received February 11, 2003
Accepted June 17, 2003

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016